410 Rec'd PCT/PTO 09 MAY 2000

SUBSTITUTE FORM PTO-1390	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTORNEY'S DOCKET NUMBER 07898-056001
TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371		U.S. APPLICATION NO. (IF KNOWN) 09/554186
INTERNATIONAL APPLICATION NO. PCT/JP99/04459	INTERNATIONAL FILING DATE August 19, 1999	PRIORITY DATE CLAIMED September 9, 1998

TITLE OF INVENTION
BIOCHIP AND METHOD FOR USING THE SAME

APPLICANT(S) FOR DO/EO/US
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Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a FIRST submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a SECOND or SUBQUENT submission of items concerning a filing under 35 U.S.C. 371.
3. ☒ This is an express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
4. ☐ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. ☒ A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. ☒ is transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☐ has been transmitted by the International Bureau.
   c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☒ A translation of the International Application (35 U.S.C. 371(c)(2)).
7. ☒ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☐ have been transmitted by the International Bureau.
   c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ☒ have not been made and will not be made.
8. ☐ A translation of amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. ☒ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
10. ☐ A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. below concern other documents or information included:

11. ☐ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. ☒ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. ☒ A FIRST preliminary amendment.
    ☐ A SECOND or SUBSEQUENT preliminary amendment.
14. ☐ A substitute specification.
15. ☐ A change of power of attorney and/or address letter.
16. ☒ Other items or information:
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I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to the Commissioner of Patents and Trademarks, Washington, D.C. 20231
Derek Norwood
Derek Norwood

U.S. APPLICATION NO. (IF KNOWN) 09/554186	INTERNATIONAL APPLICATION NO. PCT/JP99/04459	ATTORNEY'S DOCKET NUMBER 07898-056001	
17. ☒ The following fees are submitted:		CALCULATIONS	PTO USE ONLY
Basic National Fee (37 CFR 1.492(a)(1)-(5)):			
Search report has been prepared by the EPO or JPO $840		$840.00	
International preliminary examination fee paid to USPTO (37 CFR 1.482) .. $670			
No international preliminary examination fee paid to USPTO (37 CFR 1.482) but international search fee paid to USPTO (37 CFR 1.445(a)(2)) $690		$0.00	
Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO $970		$0.00	
International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(2) to (4) $96		$0.00	
ENTER APPROPRIATE BASIC FEE AMOUNT		$840.00	
Surcharge of $130 for furnishing the oath or declaration later than ☐ 20 ☐ 30 mos. from the earliest claimed priority date (37 CFR 1.492(e)).		$0.00	
Claims	Number Filed	Number Extra	Rate
Total Claims	10 - 20		x $18 = $0.00
Independent Claims	4 - 3	1	x $78 = $78.00
Multiple Dependent Claims(s) (if applicable)			+ $260 = $260.00
TOTAL OF ABOVE CALCULATIONS			$0.00
Reduction by ½ for filing by small entity, if applicable. Verified Small Entity statement must also be filed. (Note 37 CFR 1.9, 1.27, 1.28.)			$0.00
SUBTOTAL			$0.00
Processing fee of $130 for furnishing the English Translation later than ☐ 20 ☐ 30 mos. from the earliest claimed priority date (37 CFR 1.492(f))			
TOTAL NATIONAL FEE			$1,218.00
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31).			$40.00
TOTAL FEES ENCLOSED			$1,218.00
			Amount to be refunded
			Charged

a. ☒ A check in the amount of $0.00 to cover the above fees is enclosed.
b. ☐ Please charge my Deposit Account No. 06-1050 in the amount of $0.00 to cover the above fees. A duplicate copy of this sheet is enclosed.
c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 06-1050. A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b) must be filed and granted to restore the application to pending status.

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31,678
REGISTRATION NUMBER

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	: Yoshii *et al.*	Art Unit	: Unassigned
Serial No.	: To be assigned	Examiner	: Unassigned
Filed	: May 9, 2000		
Title	: BIOCHIP AND METHOD FOR USING THE SAME		

BOX PCT

Assistant Commissioner for Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Prior to examination and calculation of filing fees, please amend the application as follows:

In the Specification:

At page 8, line 2, please delete the recitation of "33b" and substitute therefor --33a--.

At page 8, line 3, please delete the recitation of "30" and substitute therefor --33--.

In the Claims:

In claim 5, line 1, please delete "claims 1-4" and substitute therefor --claim 1--.

In claim 6, line 1, please delete "claims 1-5" and substitute therefor --claim 1--.

CERTIFICATE OF MAILING BY EXPRESS MAIL

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I hereby certify under 37 CFR §1.10 that this correspondence is being deposited with the United States Postal Service as Express Mail Post Office to Addressee with sufficient postage on the date indicated below and is addressed to the Commissioner of Patents, Washington, D.C. 20231.

May 9, 2000
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Derek W. Norwood
Typed or Printed Name of Person Signing Certificate

REMARKS

The specification has been amended to address several informalities. In particular, the specification has been amended at page 8, line 2, to substitute "33b" with "33a" and at line 3 to substitute "30" with "33." The amendments were made to correctly refer to the storage medium, which is 33a, and the storage means, which is 33, in Figure 3, and is supported by the specification, for example, at page 7, second paragraph, which recites "the storage medium 33a" and the "storage means 33." Accordingly, no new matter has been added by the amendments.

Claims 5 and 6 have been amended to substitute "claims 1-4" with "claim 1" and substitute "claims 1-5" with "claim 1," respectively, in order to correct multiple claim dependency. The amendments were therefore made to address an informality and do not add new matter.

As the amendments to the specification and claims do not add new matter, Applicants respectfully request entry thereof. Applicants submit that all of the claims are now in condition for examination, which action is requested. Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date: 5/9/00

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Description

BIOCHIP AND METHOD FOR USING THE SAME

TECHNICAL FIELD

The present invention relates to a biochip having a plurality of biopolymer spots arranged thereon such as probe DNAs that specifically hybridize with a specific DNA or protein.

BACKGROUND ART

In the biochemistry research of genes or the like, conventionally and presently, biochips have been employed which are made from an immobilization support such as glass or a nylon or nitrocellurose membrane spotted with biopolymers such as DNA or protein in a high-dense pattern. Figure 2 is a schematic view of a conventional biochip. The biochip 20 is provided with an immobilization substrate 21 whose surface is spotted with various types of DNAs 22 in a predetermined pattern. Since the shapes of biochips 20 are identical, there is no way of identifying each biochip by its appearance, nor can the types of the spotted DNAs be identified. Therefore, biochips have been managed by writing an identification number 23 or by providing a barcode on the corner of the biochip 20. In this case, the biochips are managed by leaving a note of information of what kind of DNAs

are spotted on which locations on a biochip with a particular identification number or barcode.

According to the above-described method, the biochip may be identified by using two pieces of information written on separate components. However since academic information such as what kinds of nucleic acid sequences of DNAs are spotted on the chip has to be managed as another piece of information, it is often mistakenly used during the experiment.

The present invention aims at solving such problems of conventional technique, and provides a biochip whose information can unitarily be managed and provides a method for using the biochip.

DISCLOSURE OF THE INVENTION

According to the present invention, the above-described aim is accomplished by integrating a memory into a biochip so as to store information such as types, amounts and spotting locations of spotted DNAs. This biochip allows the entire information of the biochip (e.g., what kind of DNAs are spotted on which locations of the biochip, and when, by whom and in what kind of experiment the biochip was used) to unitarily be managed.

Specifically, the biochip of the invention is provided with a surface on which a plurality of biopolymers are spotted in a predetermined pattern, and a storage medium for storing information of the spotted biopolymers.

The biochip according to the present invention is provided with a surface spotted with a plurality of biopolymers such as DNAs and proteins in a predetermined pattern, and a storage medium for storing information of the biopolymers. The DNAs that are spotted on the biochip may be a plurality of probe DNAs or DNAs from individuals, which are used for genetic diagnosis or gene expression analysis.

The component with the biopolymer-spotted surface and the storage medium may be detachable from each other or they may be formed integrally. Preferably, the storage medium is a semiconductor memory capable of reading/writing information in a non-contact state.

The storage medium may be stored with information of the spotting locations on the surface of the biochip in relation to information of the biopolymers spotted on the spotting locations. The information of the spotting locations may be represented, for example, by sequential numbers of the patterned spot, or coordinates representing the spotting locations. The information of the biopolymers

to be stored may be, for example, information of nucleotide sequences of the DNAs, genetic diseases relative to the DNAs, genes relative to the DNAs, and the amounts of spots.

The biochip having the storage medium of the invention is used as follows. A plurality of biopolymers are spotted onto the surface of the biochip in a predetermined pattern. The storage medium is written with information of the spotting locations as well as information of the biopolymers (e.g., DNA nucleotide sequences) spotted on the spotting locations. The information may be written to the storage medium every time when the biopolymers are spotted, or may be written afterwards at one time.

The biochip of the invention whose surface is spotted with a plurality of biopolymers in a predetermined pattern, and which is provided with a storage medium for storing information of the spotting locations in relation to the information of the biopolymers spotted on the spotting locations, is used as follows. A sample is allowed to contact with the biochip; a spotting location that hybridized with the sample is detected by utilizing fluorescence from a fluorescent label; the database in the storage medium is searched for information of the sample-hybridized biopolymer based on the detected hybridized spotting location; and the result is displayed.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a schematic view showing an exemplary biochip of the invention;

Figure 2 is a schematic view showing a conventional biochip;

Figure 3 is a schematic view showing another exemplary biochip of the invention;

Figure 4 is a schematic view showing yet another exemplary biochip of the invention;

Figure 5 is a schematic diagram showing an example of information to be stored in the storage medium attached to the biochip;

Figure 6 is a view for illustrating the process for producing the biochip;

Figure 7 is a view for illustrating a step for inspecting the biochip;

Figure 8 is a view for illustrating hybridization process using the biochip of the invention;

Figure 9 is a view for illustrating process for reading the biochip of the invention;

Figure 10 is a view showing an example of a screen for displaying results obtained with the biochip;

Figure 11 is a view showing another example of a screen for displaying results obtained with the biochip;

Figure 12 is a diagram showing processes of reading and analyzing biochip image/memory information; and

Figure 13 is a flow chart for illustrating processes of reading and analyzing biochip image/memory information.

BEST MODE FOR CARRYING OUT THE INVENTION

Hereinafter, the present invention will be described in detail with reference to the drawings.

Figure 1 is a schematic view showing an exemplary biochip of the invention. The exemplary biochip **10** is provided with an immobilization substrate **11** (such as a glass, nylon or nitrocellulose membrane) and a storage medium **13**, the substrate **11** being spotted with biopolymers **12** (such as DNAs or proteins) at about 10,000/cm^2. The surface of the

storage medium 13 needs to be covered with plastic, glass or the like or otherwise the storage medium 13 may be exposed, together with the biopolymers 12, to a sample solution upon hybridization. The biochip 10 is made, for example, with a semiconductor memory support (such as a silicon wafer) as the immobilization substrate 11; a semiconductor memory formed on part of the support as the storage medium 13, the top of the memory being covered with a resin or the like; and biopolymers 12 such as DNAs directly spotted onto the remaining surface of the silicon support. This approach allows minimization of the biochip.

Figure 3 is a schematic view showing another example of the biochip of the invention. This exemplary biochip 30 includes a case 34 and a chip 31 whose surface is spotted with biopolymers 32 such as DNAs. The case 34 has a storage medium 33a imbedded therein, and has a cavity 35 for accommodating the chip 31. The storage medium 33a is an IC memory which is connected to a looped antenna 33b which is also imbedded in the case 34, thereby forming a non-contact storage means 33.

The non-contact storage means 33 receives an electromagnetic wave sent from a reader/writer located close to the biochip 30 via the antenna 33b. An electromotive force generated by electromagnetic induction is used as

electric power for data communication to write/read information to/from the storage medium 33b. The non-contact storage means 30 reads/writes information in a non-contact state without requiring an externally exposed terminal and thus is completely enclosed and isolated from the external environment. Accordingly, the non-contact storage means 33 is preferable as a memory for a biochip that is exposed to a reagent or a sample solution.

The biochip 30 shown in Figure 3 is used generally as follows. The process for spotting biopolymers onto the biochip 30 is conducted with only the chip 31 separated from the case 34. Then, the chip 31 is fit into the cavity 35 of the case 34 to form an integral body. The integrated biochip 30 is subjected to a later-described inspection step shown in Figure 7 to write inspection information to the memory medium 33a of the non-contact storage means 33. Then, the chip 31 is separated from the case 33 and immersed into a hybridization solution to perform a later-described hybridization reaction step shown in Figure 8. After the hybridization reaction, the chip 31 is again assembled with the case 34 to perform a later-described reading process shown in Figure 9. Data obtained through the reading process is stored into the storage medium 33a of the non-contact storage means 33.

According to the biochip **30** of a system shown in Figure **3**, the case **34** provided with the non-contact storage means **33** is not exposed to a solution during the hybridization reaction. Accordingly, there is less limitation as to the material used for the case **34**. Since the case **34** is not exposed to a solution, a contact-type storage means whose terminals and the like are exposed above the surface of the case may be used instead of the non-contact storage means **33**. The case **34** may be reused by deleting the stored data in the storage medium **33a**.

Figure **4** is a schematic view showing another example of a biochip of the invention. This exemplary biochip **40** is produced by: partially forming a cavity in an immobilization substrate **41** (such as glass or plastic) by an etching process or the like; placing a non-contact storage means **43** made from a looped antenna **43b** and a storage medium **43a** connected thereto; and imbedding the storage medium **43a** with a resin or the like. The surface of the immobilization substrate **41** is spotted with biopolymers **42** such as DNAs in a predetermined pattern. The biochip of such a system has a simple mechanism as compared to the biochip shown in Figure **3**. Since the storage medium is integrally imbedded in the material to be spotted with the biopolymers, the entire biochip may be minimized.

Figure 5 is a diagram showing an example of information to be stored in a storage medium for a single biochip. The information to be stored include general information of the biochip such as a serial number, a fabrication lot number, date/time of preparation, the number of spots on the biochip, and other additional chip information, as well as information of respective spots on the biochip. The information of respective spots on the biochip include, for example, spot numbers, X-Y-coordinates on the biochip, spotting conditions such as amount and time of spotting, and additional information such as names and functions of the spotted DNAs or proteins. The spot numbers are sequentially provided in accordance with the order of spotting. The X-Y coordinates are represented, for example, while the origin is at the upper left corner of the biochip. When the biochip is used for DNA diagnosis, information of an individual and information usually written in a clinical record may also be stored.

A method for managing information in the chip will be described with reference to Figures 6 to 9. Figure 6 is a view for illustrating process for producing the biochip. A microplate 61 has various biopolymers (for example, sample DNAs 62 having known nucleotide sequences) placed at known respective locations. Under the control of a drive controller 65 controlled by a computer 66, a pin 64 is

transferred to a predetermined location on the microplate 61 with an X-Y driver 63 and made to contact at the tip thereof with the DNA at that location. The pin 64 is again transferred to a predetermined location on the biochip 1 to spot the DNA onto the surface of the chip, thereby forming a DNA spot 2 on the biochip 1. By repeating this action, each sample DNA 62 on the microplate 61 will be spotted onto the biochip 1 in a predetermined pattern. The biochip 1 is provided with a memory 3.

The computer 66 commands a reader/writer 67 to write to the memory 3, spot numbers, spotting locations, nucleic acid sequences of the sample DNAs 62 applied to the spotting locations, name of the genes, the number and location of the microplate 61 and preparation date of the biochip 1, for example, as in a format shown in Figure 5. The reader/writer 67 is preferably of a non-contact type, but may be a contact-type for biochips such as one shown in Figure 3. The information may be written with the reader/writer 67 one at a time synchronous with the spotting operation or at one time after completing the entire spotting manipulation.

Figure 7 is a view for illustrating a step for inspecting the biochip. In this step, the biochip 1 produced through the process shown in Figure 6 is subjected to an inspection of, for example, whether the DNAs are spotted

appropriately onto all of the spotting locations 2. The inspection results are written to the memory 3 of the biochip.

An image of the spot arrangement on the biochip 1 is taken with an image pick-up camera 71 such as a CCD camera and the image data is transferred to the computer 66 via a reading controller 72. The computer 66 analyzes the image data of the spot arrangement to detect defective spots where an amount of spotted DNA is inadequate. All of the sample DNAs 62 on the microplate 61 may be provided with a fluorescent material such as FITC (fluorescein isothiocyanate), in which case spot points 2 may be irradiated with excitation light from an argon ion laser or the like, so as to detect defective spots based on the presence and absence of the fluorescent light from the fluorescent material at each spotting location. The fluorescent intensity from each spot may also be measured so as to detect the amount of DNA spotted onto each spot. The spot number of the defective spot, the amount of DNA spotted onto each spot may be written to the memory 3 with the reader/writer 67 under the control of the computer 66.

After the inspection step shown in Figure 7, the DNA of the defective spot may be spotted again by the spotting step shown in Figure 6. In this case, the location to be spotted again may be the same as the location found to be defective

or may be at an alternative location different from the first spotting location. Furthermore, instead of directly taking the image of the spot arrangement on the biochip, it may be taken via a phase contrast microscope.

Figure 8 is a view for illustrating a hybridization process using the biochip of the invention. As shown in the figure, the biochip 1 provided with the storage medium 3 and the biopolymers 2 such as DNAs, together with fluorescent-labeled sample DNA 82, is placed into a hybridization solution 81 for hybridization. When there is a complementary DNA sequence between the DNA 2 spotted on the biochip 1 and the sample DNA 82, the DNAs bind to each other and form a duplex structure on the spot.

Figure 9 is a view for illustrating the reading and analyzing processes of the biochip of the invention. The DNA of the spot 2 on the biochip 1 which has bound with the sample DNA is detected by radiating excitation light to the spots 2 on the biochip 1 and reading the fluorescence emitted from the spot with an optical sensor (such as a CCD 71). The data read with the optical sensor is transferred to the computer 66 via the reading controller 72. The computer 66 uses information of the fluorescence location on the biochip 1 read with the optical sensor, and information of the spot read from the memory 3 of the biochip 1 using the

reader/writer 67, thereby deriving information of the sample DNA on the biochip that hybridized with the DNA. Specifically, from the results read with the optical sensor, the information in the memory 3 corresponding to the DNA on the biochip 1 which is suspected to have hybridized is output to the display of the computer 66.

The data is normalized based on the difference between the data of the amount of the DNA of the spot stored in the memory 3 and the amount of the DNA that hybridized obtained with the optical sensor. The results are written to the memory 3 with the reader/writer 67. Accordingly, the information can unitarily be managed. In addition, quantitative analyasis and expression level analysis are also possible.

Figures 10 and 11 are views showing exemplary screens displaying analysis results obtained with the biochip as described with reference to Figure 9. The exemplary screen shown in Figure 10 displays fluorescent intensity image of the biochip read with the optical sensor. When the operator points the image of the spot that (s)he wants to know in detail (e.g., with a mouse cursor), the additional information stored in the memory will be read out with the reader/writer 67 and displayed on the screen.

The exemplary screen shown in Figure 11 displays the analysis results in a list format. Referring to Figure 11, identification and additional information of the biochip, information of each spot and the results of the hybridization reaction are displayed. The hybridization reaction results are shown as ○ for those that went through hybridization, or × for those that did not cause hybridization. Although information of all of the spots is displayed according to this example, the results may be displayed, after an appropriate filtering process, for example, with a list of only the spots that went through hybridization. The screens shown in Figures 10 and 11 may alternately be displayed from one another.

Figure 12 is a diagram illustrating a series of processes for using the biochip. A biochip image/memory information reading program 90 loaded into the computer 66 is initiated as instructed via an input device such as a keyboard 101. An image reading module 91 of the biochip image/memory information reading program 90 loaded into the computer 66 controls a reading controller 72 of a biochip reader 70 and reads the fluorescent intensities of the spots 2 on the biochip 1 with an optical sensor such as a CCD 71. The image data read out is transferred from the reading controller 72 to the computer 66. The transferred image data is subjected to noise elimination and peak recognition

processes with a noise filtering module 92 and an image peak recognizing module 93, respectively, thereby determining the peak coordinates and intensity of the fluorescence at each spot.

Then, the memory information reading module 94 instructs the biochip reader 70 to read spot information stored in the memory 3 on the biochip 1. The spot information read out is transferred to the computer 66. An image/memory information corresponding module 95 corresponds the spot information with information of the image data, peak coordinates and fluorescent intensity. An image/memory information screen displaying module 96 displays the corresponded image/memory information on an RGB display 102. An image/memory information storing module 97 stores the image/memory information in a storage medium 110 such as a hard disk device 111, a floppy disk device 112 or the biochip 1. Each of the modules shown in Figure 12 may be realized by a software program.

Figure 13 is a flow chart for illustrating processes of reading and analyzing biochip image/memory information. The reading device and the like are initialized, followed by chip image reading process (S11) for reading fluorescent intensities of spots 2 on the biochip 1 with the optical sensor such as the CCD 71; process (S12) for reading spot

information stored in memory 3 of the biochip 1; process (S13) for recognizing peak coordinates and peak intensities of the fluorescence of the spots of the chip image; and process (S14) for corresponding the spot peak information obtained from the chip image and the spot information stored in the memory. The information obtained through such a series of process, according to the selected display format at S15, is subjected to process for displaying the chip image and information of a spot at a cursor point (S16) or to process for displaying the list of spot intensities and spot information (S17). The chip image, spot intensities and spot information are stored in a storage medium such as the hard disc device 111, the floppy disc device 112 or the biochip 1. Thus, a terminating process terminates the reading/analyzing process of the biochip image/memory information.

The biochip of the invention provided with a memory allows unitary management of information by storing data of, for example, a sample DNA and experimental environment used for the biochip, as well as the results of an analysis or the like in the memory. Accordingly, an experimental error can be avoided. Moreover, accurate experimental results can be obtained if information of an amount of each of the DNAs on the chip is stored in the memory in advance such that the results are obtained based on the difference from the amount of DNA upon chip reading after the hybridization experiment

or the like. In the case where the results of the analysis are managed as a database, the information may directly be read from the memory so that information may be managed in a facilitated manner.

INDUSTRIAL APPLICATION

According to the present invention, unitary management of information is realized by storing information of a biochip in the biochip itself, thereby preventing errors and realizing rapid and accurate process.

Claims

1. A biochip comprising a surface to be spotted with a plurality of biopolymers in a predetermined pattern, and a storage medium for storing information of the biopolymers to be spotted.

2. A biochip comprising a surface spotted with a plurality of biopolymers in a predetermined pattern, and a storage medium for storing information of the biopolymers.

3. A biochip according to claim 1 or 2, wherein a member provided with the surface and the storage medium are detachable.

4. A biochip according to claim 1 or 2, wherein a member provided with the surface and the storage medium are formed integrally.

5. A biochip according to any one of claims 1-4, wherein the storage medium is a semiconductor memory which can read/write information in a non-contact state.

6. A biochip according to any one of claims 1-5, wherein the storage medium stores information of the spot locations on the surface in relation to information of the biopolymers

spotted on the spot locations.

7. A method for using a biochip, wherein a plurality of biopolymers are spotted on a surface of the biochip in a predetermined pattern, the biochip being provided with a storage medium; and wherein information of the spot locations are written to the storage medium in relation to information of biopolymers spotted on the spot locations.

8. A method for using a biochip, comprising the steps of:

applying a sample to the biochip whose surface is spotted with a plurality of biopolymers in a predetermined pattern; and

detecting a spot location where the sample has hybridized,

wherein the biochip is provided with a storage medium that stores information of the spot locations in relation to information of biopolymers spotted on the spot locations, and wherein information of the biopolymer that has hybridized with the sample is searched in the data stored in the storage medium based on the hybridized spot location and is displayed.

ABSTRACT

The invention provides a biochip that allows unitary management of information, and a method for using the same. An immobilization substrate (11) such as a glass substrate spotted with biopolymers (12) such as DNAs or proteins is provided with a storage medium (13) for storing information of spot locations on the biochip (10) and information of the spotted biopolymer at each spot location.

FIG.1

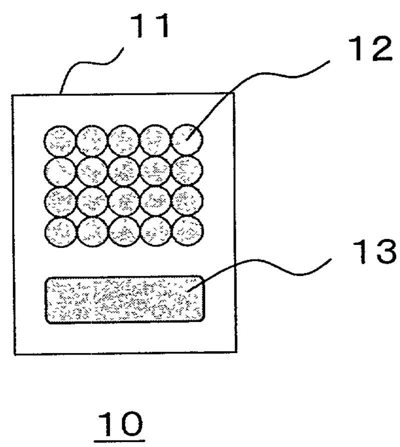


FIG.2

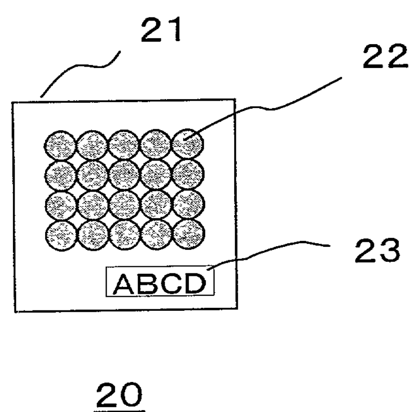


FIG.3

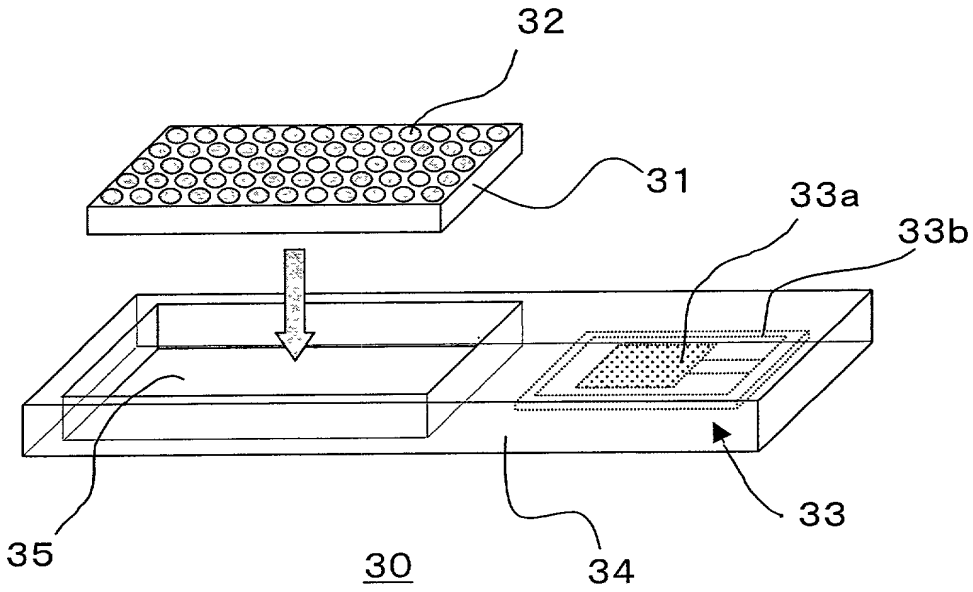


FIG.4

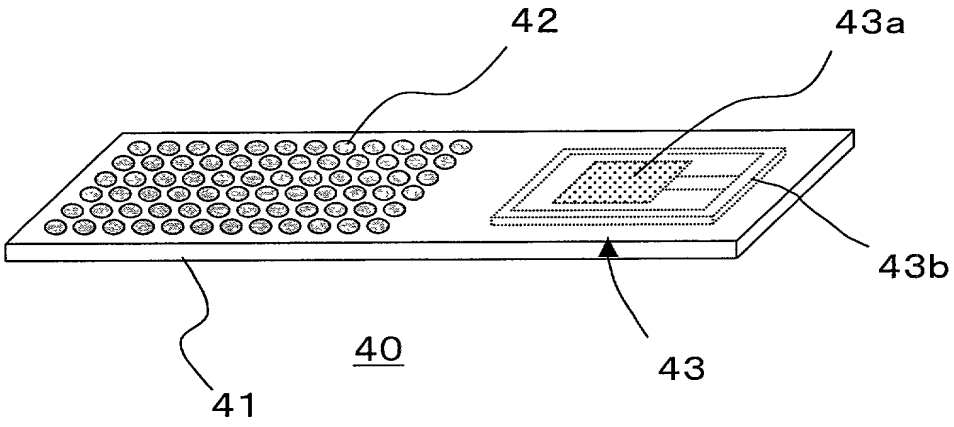


FIG.5

Chip number			
Fabrication lot number			
Date/time of preparation			
Number of spots (n)			
Additional chip information			
Spot No. (1)	Spotting location [coordinates (x1,y1)]	Spotting condition information (1)	Additional spotting information (1)
(2)	[coordinates (x2,y2)]	(2)	(2)
⋮	⋮	⋮	⋮
(n)	[coordinates (xn,yn)]	(n)	(n)

FIG.6

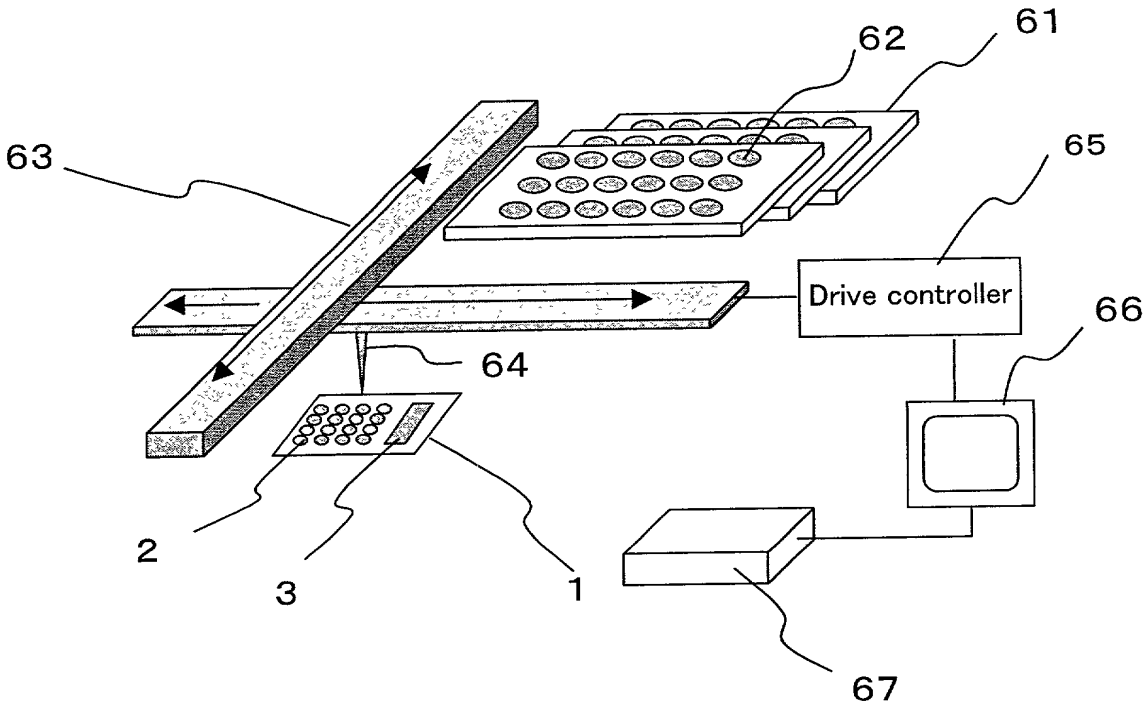

62
61
63
65
Drive controller
66
64
2
3
1
67

FIG.7

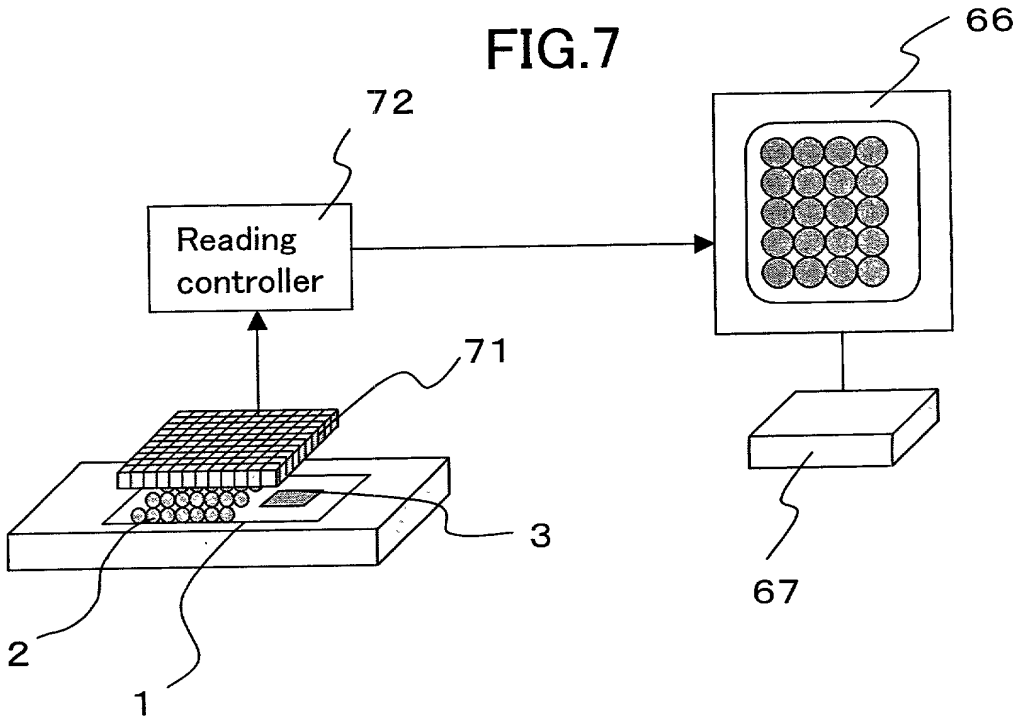

66
72
Reading controller
71
3
2
1
67

FIG.8

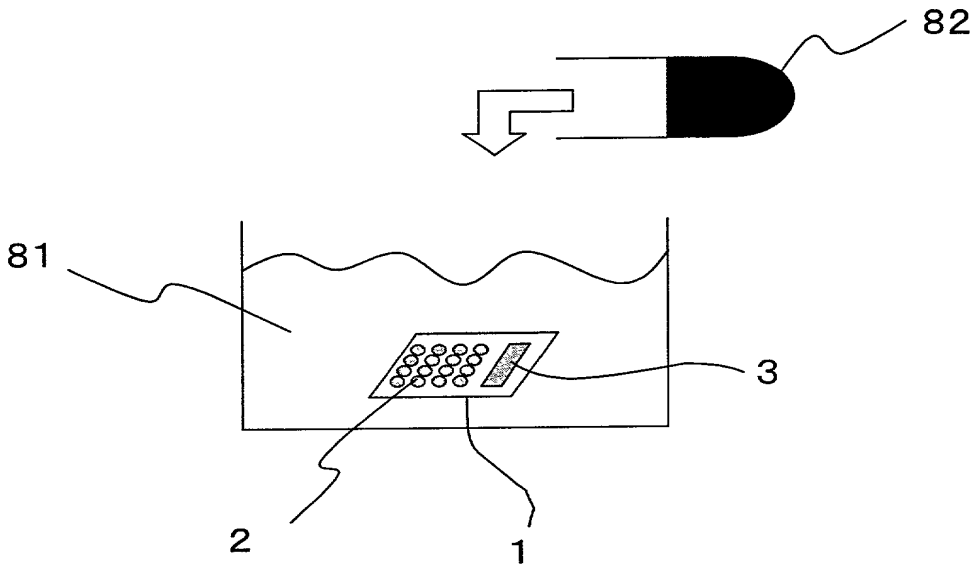


FIG.9

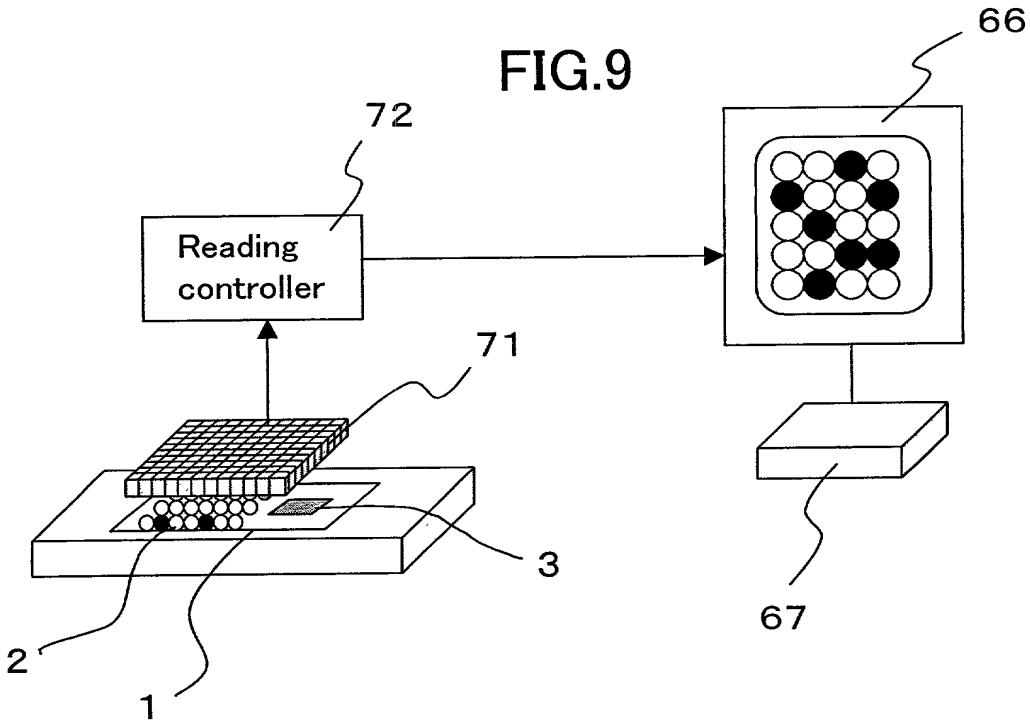


FIG.10

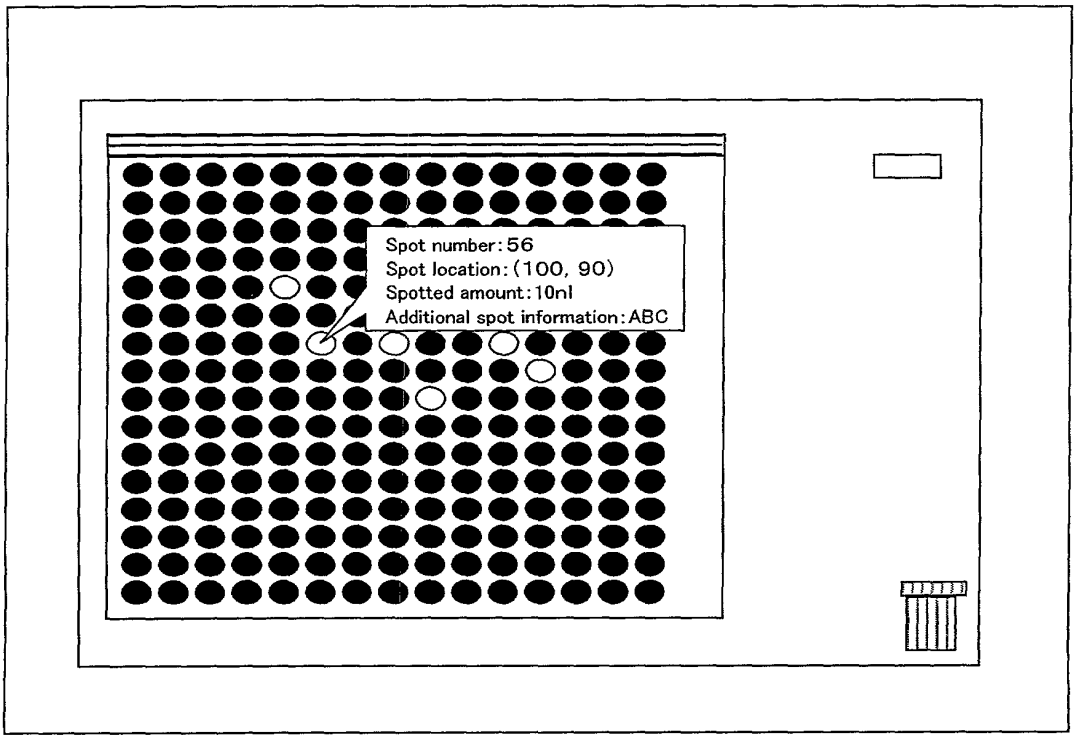

Spot number: 56
Spot location: (100, 90)
Spotted amount: 10nl
Additional spot information: ABC

FIG.11

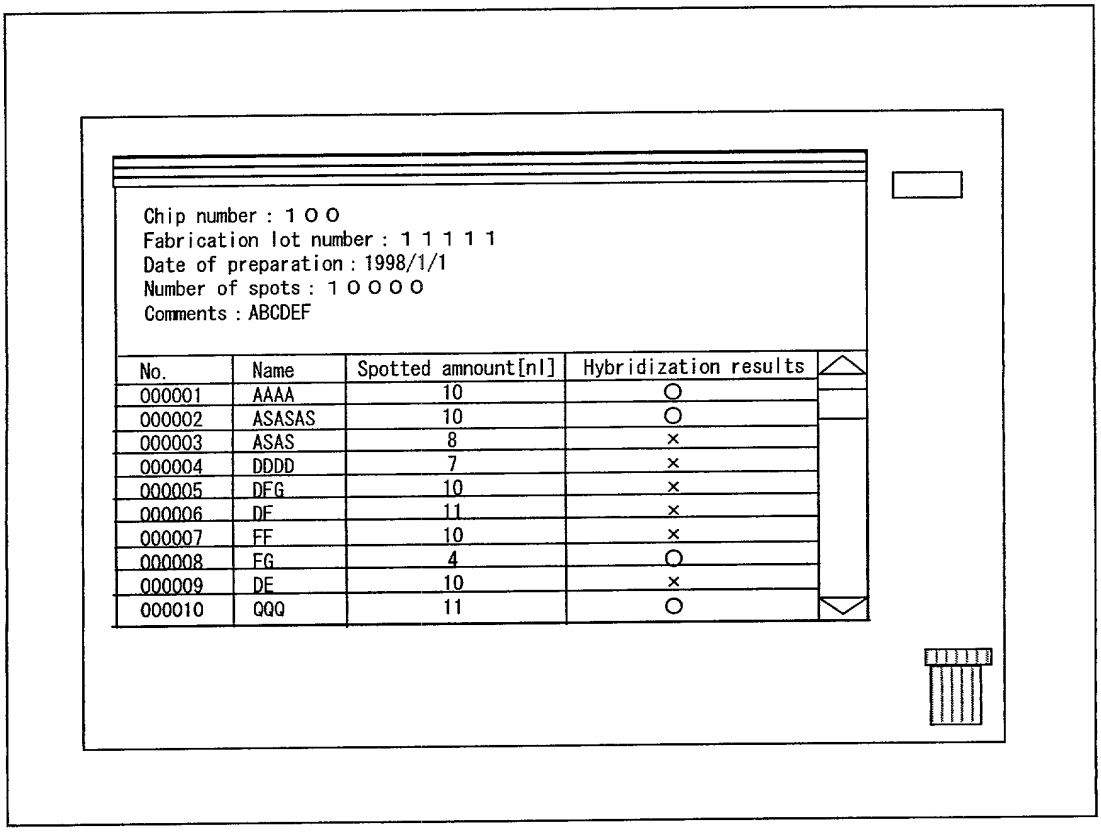

Chip number : 1 0 0
Fabrication lot number : 1 1 1 1 1
Date of preparation : 1998/1/1
Number of spots : 1 0 0 0 0
Comments : ABCDEF
No. | Name | Spotted amnount[nl] | Hybridization results
000001 | AAAA | 10 | ○
000002 | ASASAS | 10 | ○
000003 | ASAS | 8 | ×
000004 | DDDD | 7 | ×
000005 | DFG | 10 | ×
000006 | DF | 11 | ×
000007 | FF | 10 | ×
000008 | FG | 4 | ○
000009 | DE | 10 | ×
000010 | QQQ | 11 | ○

FIG.12

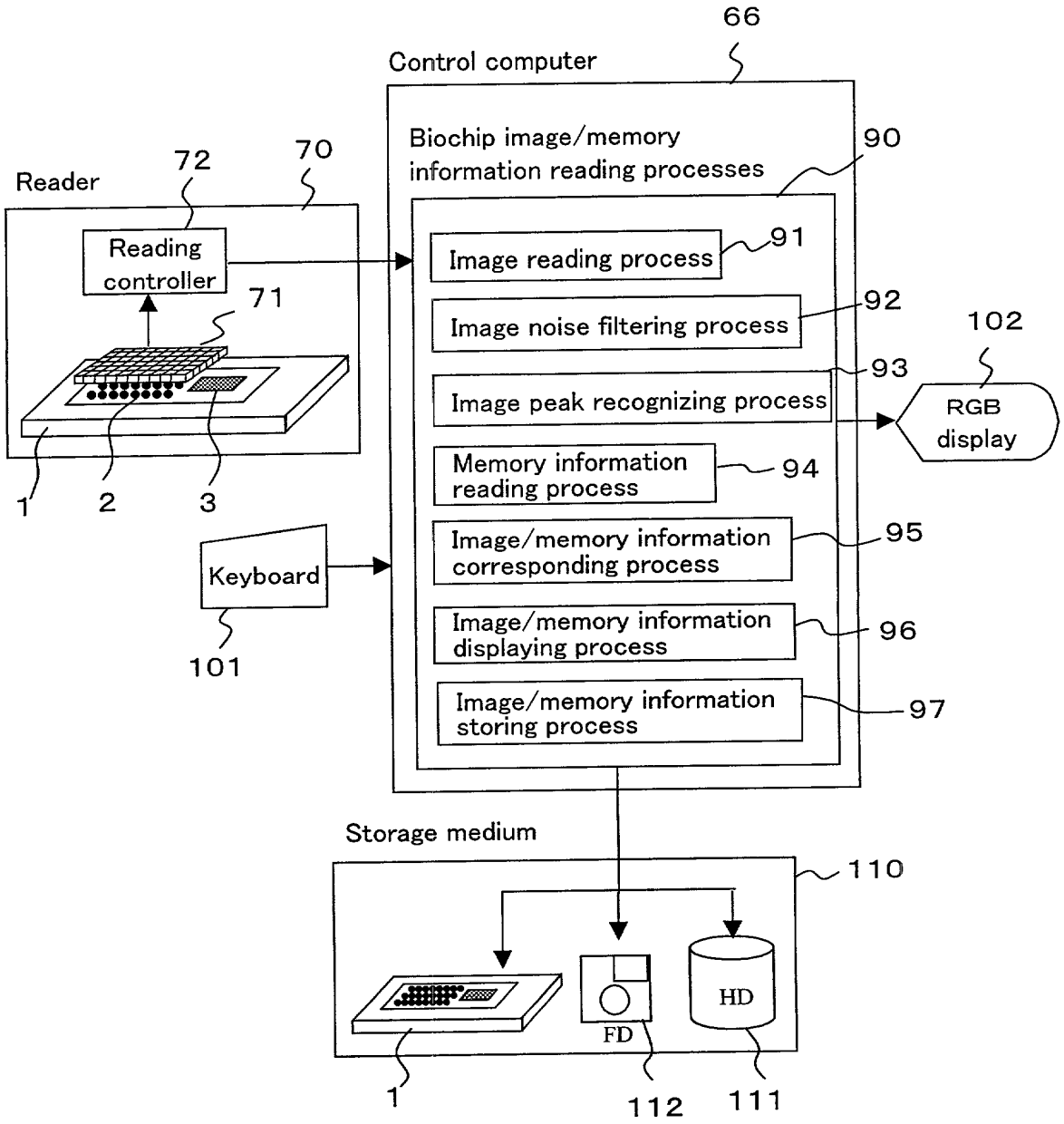
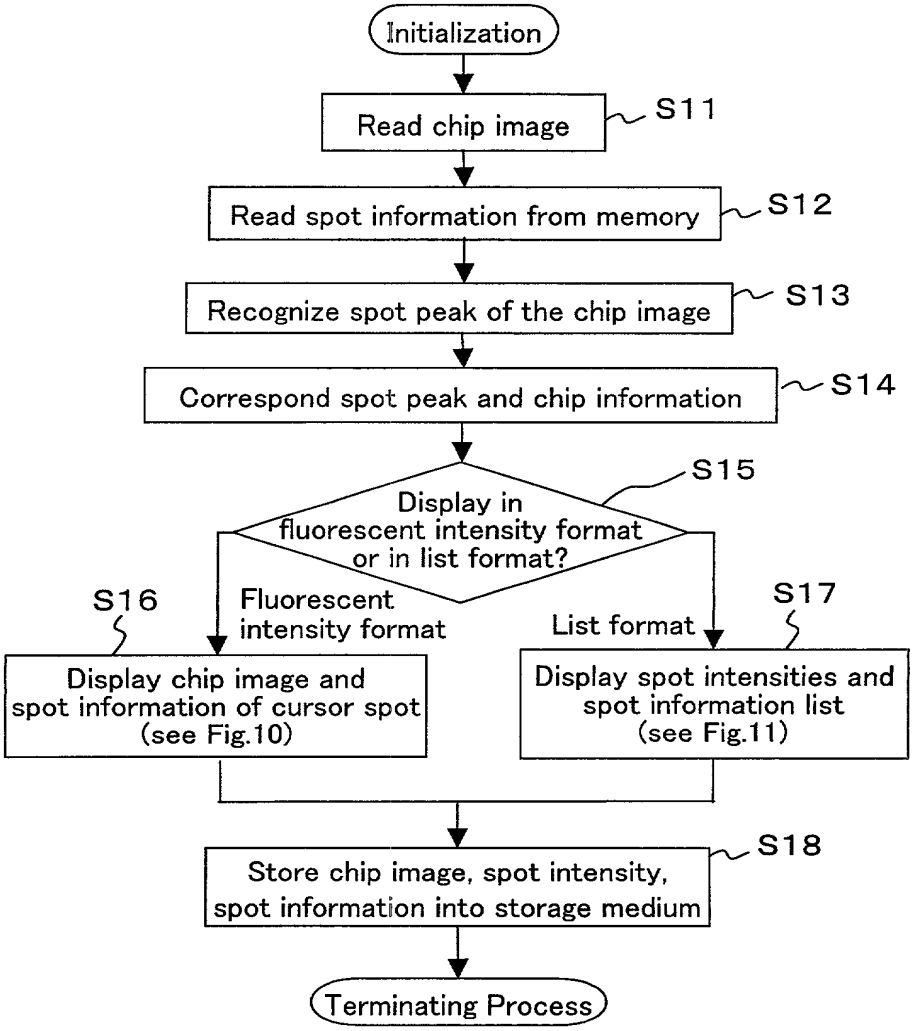

66
Control computer
Biochip image/memory information reading processes
90
Reader
72
70
Reading controller
71
1
2
3
Image reading process
91
Image noise filtering process
92
Image peak recognizing process
93
102
RGB display
Memory information reading process
94
Image/memory information corresponding process
95
Image/memory information displaying process
96
Image/memory information storing process
97
Keyboard
101
Storage medium
110
FD
HD
1
112
111

FIG.13


Initialization
Read chip image
S11
Read spot information from memory
S12
Recognize spot peak of the chip image
S13
Correspond spot peak and chip information
S14
Display in fluorescent intensity format or in list format?
S15
S16
Fluorescent intensity format
List format
S17
Display chip image and spot information of cursor spot (see Fig.10)
Display spot intensities and spot information list (see Fig.11)
Store chip image, spot intensity, spot information into storage medium
S18
Terminating Process

Attorney's Docket No.: 07898-056001

DECLARATION, POWER OF ATTORNEY AND PETITION

I (We), the undersigned inventor(s), hereby declare that:

My residence, post office address and citizenship are as stated below next to my name,

I (We) believe that I am (we are) the original, first, and joint (sole) inventor(s) of the subject matter which is claimed and for which a patent is sought on the invention entitled

BIOCHIP AND METHOD FOR USING THE SAME

the specification of which

- ☐ is attached hereto.
- ☐ was filed on _____ as Application Serial No. _____ and amended on _____.
- ■ was filed as PCT international application Number PCT/JP99/04459 on August 19, 1999, and was amended under PCT Article 19 on _____ (if applicable).

I (We) hereby state that I (We) have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above; that I (We) do not know and do not believe that this invention was ever known or used before my invention or discovery thereof, or patented or described in any printed publication in any country before my invention or discovery thereof, or more than one year prior to this application, or in public use or on sale in the United States for more than one year prior to this application; that this invention or discovery has not been patented or made the subject of an inventor's certificate in any country foreign to the United States on an application filed by me or my legal representatives or assigns more than twelve months before this application.

I (We) acknowledge the duty to disclose information known to be material to the patentability of this application as defined in Section 1.56 of Title 37 Code of Federal Regulations.

I (We) hereby claim foreign priority benefits under Section 119(a)-(d) of Title 35 United States Code, of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

Application No.	Country	Filing date	Priority claimed
255288/1998	Japan	September 9, 1998	■ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No

I hereby claim the benefit under Section 119(e) of Title 35 United States Code, of any United States application(s) listed below.

(Application Number)	(Filing Date)
(Application Number)	(Filing Date)

I (We) hereby claim the benefit under Section 120 of Title 35 United States Code, of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Section 112 of Title 35 United States Code, I (We) acknowledge the duty to disclose material information as defined in Section 1.56(a) of Title 37 Code of Federal Regulations, which occurred between the filing date of the prior application and national or PCT international filing date of this application:

Application Serial No.	Filing Date	Status (pending, patented, abandoned)

And I (We) hereby appoint: William E. Booth, Registration No. 28,933; Margaret A. Boulware, Registration No. 28,708; Karl Bozicevic, Registration No. 28,807; Barry E. Bretschneider, Registration No. 28,055; Paul T. Clark, Registration No. 30,162; Peter J. Devlin, Registration No. 31,753; William J. Egan, Registration No. 28,411; Willis M. Ertman, Registration No. 18,658; David L. Feigenbaum, Registration No. 30,378; Janis K. Fraser, Registration No. 34,819; John W. Freeman, Registration No. 29,066; Timothy A. French, Registration No. 30,175; Alan H. Gordon, Registration No. 26,168; Scott C. Harris, Registration No. 32,030; Mark J. Hebert, Registration No. 31,766; Gilbert H. Hennessey, Registration No. 25,759; Charles Hieken, Registration No. 18,411; Robert E. Hillman, Registration No. 22.837; John F. Land, Registration No. 29,554; G. Roger Lee, Registration No. 28,963; Steven E. Lipman, Registration No. 30,011; Gregory A. Madera, Registration No. 28,878; Ralph A. Mittelberger, Registration No. 33,195; Ronald E. Myrick, Registration No. 26,315; Robert C. Nabinger, Registration No. 33,431; Frank P. Porcelli, Registration No. 27,374; Eric L. Prahl, Registration No. 32,590; Alan D. Rosenthal, Registration No. 27,833; Richard M. Sharkansky, Registration No. 25,800; John M. Skenyon, Registration No. 27,468; Michael O. Sutton, Registration No. 26,675; Reginald J. Suyat, Registration No. 28,172; Rene D. Tegtmeyer, Registration No. 33,567; Hans R. Troesch, Registration No. 36,950; John R. Wetherell, Registration No. 31,678; Wayne E. Willenberg, Registration No. 28,488; John N. Williams, Registration No. 18,948; Gary A. Walpert, Registration No. 26,098; Dorothy P. Whelan, Registration No. 33,814; and Charles C. Winchester, Registration No. 21,040; John R. Wetherell, Jr., Registration No. 31,678; John W. Freeman, Registration No. 29,066; Scott C. Harris, Registration No. 32,030; John F. Land, Registration No. 29,554; and Hans R. Troesch, Registration No. 36,950.

I(We) hereby request that all correspondence regarding this application be sent to the firm of FISH & RICHARDSON P.C. whose Post office address is: 4350 La Jolla Village Drive, Suite 500, San Diego California 92122 U.S.A.

I (We) declare further that all statements made herein of my (our) knowledge are true and that all statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

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Date